

**Statistical Analysis of the Diagnostic Accuracy of Morphological
Features in the Cytological Diagnosis of
Proliferative Breast Lesions**

Fine Needle Aspiration Compared to Histological Diagnosis

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Certificate of Authorship

I certify that the substance of this thesis has not been submitted already for any degree and is not being submitted currently for any other degree.

I certify that any help received in preparing this thesis, and all sources used, have been acknowledged. In addition, I certify that all information sources and literature used are indicated in the thesis.

Signature of Candidate

A handwritten signature in black ink, appearing to be 'Alison', written over a horizontal line.

Alison Ching Fong Mak

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List of Abbreviations for Non-cytological Criteria

aden	adenosis
ADH	atypical ductal hyperplasia
ALH	atypical lobular hyperplasia
Ca	carcinoma
CIPL	complex intraduct papillary lesion
col cell hyperpl	columnar cell hyperplasia
CSL	complex sclerosing lesion
DCIS	ductal carcinoma <i>in situ</i>
DD	differential diagnosis
EH	epithelial hyperplasia
EHA	epithelial hyperplasia with atypia
FA	fibroadenoma
FCC	fibrocystic change
FHWA	florid epithelial hyperplasia with atypia
FNAB	fine needle aspiration biopsy
intra comp	intraduct component
L	left/lower
LCIS	lobular carcinoma <i>in situ</i>
LG	low grade
ND	not diagnostic of a specific lesion
NEOM	no evidence of malignancy
NI	not indicated
NOS	not otherwise specified
O	outer
pap Ca	papillary carcinoma
pap	papilloma
PBL	proliferative breast lesion
PL	papillary lesion
PPV	positive predictive value

List of Abbreviations for Non-cytological Criteria (continued)

PSB	proteinaceous material
Q	quadrant
R	right
RS	radial scar
SBC	Sydney Breast Clinic
scler	sclerosing
SF	stromal fragment
TC	tubular carcinoma
TF	tissue fragment
U	upper

List of Abbreviations for the Cytological Criteria

aniso	nuclear size variation
antler	antler horn, drumstick tissue fragments
apo sheet	apocrine sheets
atyp disp	dispersed atypical cells
BBN	bare bipolar nuclei
Ca ²⁺ epith	psammomatous calcifications – in epithelium
Ca ²⁺ in pap	psammomatous calcifications in papillary fragments
Ca ²⁺ stroma	psammomatous calcifications – in stroma
chromatin	nuclear pleomorphism of chromatin
cohesion	cohesion vs discohesion
coll spher	collagenous spherulosis
comp EH	cohesive tissue fragments folded, mildly complex, branched with myoepithelial cells; may show some apocrine differentiation
disorg frond	more complex papillae with thin disorganized fronds
disp + TF	largely dispersed cells with scattered small or large tissue fragments
disp apo	dispersed apocrine cells
disp epith	dispersed epithelial cells
dispersed	dispersed cells with a few small discohesive tissue fragments of 5-20 cells
FA stroma	rounded, club ended, “clover leaf”, smooth edged – “fibroadenoma” stroma
free Ca ²⁺	psammomatous calcifications – free
free gran	granular calcifications – free
hard-edge	three dimensional, round, hard-edged, branched tissue fragments
hypercell	hypercellular (“cellular fibroadenoma”) stroma
hyperchrom	nuclear hyperchromasia
L+S	large tissue fragments with scattered small tissue fragments with bare bipolar nuclei and few dispersed cells
large ball	large rounded, balled up, isolated tissue fragments
large nucleo	single and large nucleoli

List of Abbreviations for the Cytological Criteria (continued)

large TF	large tissue fragments with bare bipolar nuclei and few dispersed cells
long strip	columnar cells in long strips/palisading arrays (>6 cells)
MEC	myoepithelial cells within tissue fragments
meshwork	“meshwork” – thin stroma surrounding tubules/acini/epithelial clumps/nests
mitosis	mitoses
mix	mix of large and small tissue fragments with bare bipolar nuclei and some dispersed cells
multi nucleo	multiple nucleoli
myxoid	myxoid stromal fragments typical of FA
naked aty	stripped, enlarged atypical nuclei
necrosis	granular necrosis
normal st	unremarkable stromal fragments with some spindly nuclei
nuclei enlarge	nuclear enlargement
old bl/sid	old blood with or without siderophages
pap large tip	papillae – micropapillary with no visible fibrovascular core (tips larger than base)
pap w FVC	papillae – with visible fibrovascular core (papillary fragments)
pap wo FVC	papillae – three dimensional structure with no visible fibrovascular core
PSB	proteinaceous material without cells
PSB/mos	proteinaceous material with foamy macrophages
PSB/mos/sid	proteinaceous material with foamy macrophages and siderophages
PSB/sid	proteinaceous material with siderophages
ragged dis	ragged, discohesive tissue fragments
ragged tuft	small ragged stromal fragments – “tufts”
short strip	columnar cells in short strips/palisading arrays (<6 cells)
sing col	single columnar cells
small ball	small rounded, balled up, isolated tissue fragments
small EH	small tissue fragments and sheets with myoepithelial cells

List of Abbreviations for the Cytological Criteria (continued)

small nucleo	single and small nucleoli
small TF	small tissue fragments and scattered large tissue fragments with bare bipolar nuclei or some dispersed cells
stellate	branched, stellate stromal fragments with small epithelial tissue fragments attached
tubular	tubular structure

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Abstract

Cytological features of the various proliferative breast lesions have been described by numerous authors. The aim of this study was to evaluate the usefulness of these criteria in diagnosing epithelial hyperplasia with atypia (EHA), papillary lesions (PLs) and radial scar/complex sclerosing lesions (RS/CSLs) by fine needle aspiration biopsy (FNAB). EHA is a cytological diagnosis that raises a histological differential diagnosis of florid epithelial hyperplasia, atypical ductal hyperplasia and low-grade ductal carcinoma *in situ*. Papillary lesions in this study refer to intraduct papillomas of varying types including complex intraduct papillary lesions (CIPLs).

This study comprised both retrospective and prospective components. In the retrospective component, 77 cases found to be suitable for the study, were reviewed. They comprised 13 cases of EHA, 52 cases of PLs and 12 cases of RS/CSL. Cytological criteria were extracted from the literature, together with in-house criteria, which have been developed and used at the St. Vincent's Hospital, Sydney. Slides were reviewed and scored against these criteria. The results were analysed statistically to test if there was a significant association between the cytological criteria and the histological outcomes.

As the number of cases for the groups of EHA and RS/CSL were small compared to PLs, they were grouped together in the statistical analysis. One of the most significant findings was that the presence of stellate or meshwork stromal fragments is highly predictive of a PL. Papillary fragments were found infrequently and were of limited use in making the diagnosis of a PL, which is in contradiction to much of the literature.

The prospective part of the study aimed to test the sensitivity, specificity and positive predictive value of the criteria evaluated in the retrospective study in the diagnosis of PLs. Of the 1154 cases collected, 74 were suitable for slide review and scoring.

It was again found that meshwork stromal fragments occurred most frequently in PLs followed by stellate stromal fragments, whereas papillary fragments had the lowest

occurrence. However, all of these three criteria were found to be highly specific for PLs. The co-existence of either a proteinaceous background with macrophages and siderophages, or moderate to marked apocrine sheets further increased their specificities and positive predictive values.